REMARKS

Claims 1-28 are pending in the application. Claims 3, 6, 7, 13-21, and 24-26 are withdrawn. Claims 1, 2, 4, 5, 8-12, 22, and 23 are pending and presently stand rejected. Claims 1 and 11 have been amended. New claims 27 and 28 have been added.

Rejections under 35 USC §102

Claims 1 and 8-10 were rejected under 35 USC §102(b) as being anticipated by US 5,665,582 to **Kausch**. Applicants have amended claim 1 to include the limitations of the original dependent claim 2. Claim 1, as amended, calls for a nucleic binding portion for attracting and non-covalently and non-sequence specifically binding nucleic acids and wherein the nucleic acid binding portion includes a ternary or quaternary onium group. **Kausch** does not identically disclose a nucleic acid binding portion as recited in amended claim 1. The amendment renders the rejection under 35 USC 102 moot and withdrawal of the rejection is respectfully rejected.

Claims 1, 8, 9, and 12 were rejected under 35 USC §102(b) as being anticipated by US 6,060,246 to **Summerton**. Applicants have amended claim 1 to include the limitations of the original dependent claim 2. Claim 1, as amended, recites a nucleic binding portion for attracting and non-covalently and non-sequence specifically binding nucleic acids and wherein the nucleic acid binding portion includes a ternary or quaternary onium group. **Summerton** does not identically disclose a nucleic acid binding portion as recited in amended claim 1. The amendment renders the rejection under 35 USC 102 moot and withdrawal of the rejection is respectfully rejected.

Claims 1 and 8 were rejected under 35 USC §102(b) as being anticipated by US 5,900,481 to **Lough**. This reference discloses use of an oligonucleotide-labeled bead immobilized on a solid support. Applicants have amended claim 1 to include the limitations of the original dependent claim 2. Claim 1, as amended, recites a nucleic binding portion for attracting and non-covalently and non-sequence specifically binding nucleic acids and wherein the nucleic acid binding portion includes a ternary or quaternary onium group. **Lough** does not identically disclose a nucleic acid binding portion as recited in amended claim 1. The amendment renders the rejection under 35 USC 102 moot and withdrawal of the rejection is respectfully rejected.

Rejections under 35 USC §103

Claims 1, 2, 4, 8, and 11 were rejected under 35 USC § 103(a) as being unpatentable over U.S. 5,900,481 to **Lough** and a paper (Tetrahedon Lett., 37: 7595-7598 (1996) **Hughes**). This rejection is traversed on several grounds.

1) The Examiner's characterization of the teaching of Hughes as disclosing "hydrolysis of an aralkyl quaternary phosphonium ylide (salt) from a solid matrix" is incorrect. In fact, the polymer-bound triphenylphosphine is used as a support for "traceless synthesis". Its function is to serve as a scaffold upon which to temporarily link a molecule in order to perform some synthetic elaboration on it to form a new molecule and then remove the new molecule from the linker without it bearing any trace of the solid phase linker. It is inherent in this example that the phosphorus is never cleaved from the solid phase. Linking the reactant molecule to the triphenylphosphine resin creates a

phosphonium group. Cleaving the new molecule recreates the original triphenylphosphine resin. The phosphonium salt at no time is freed from the polymer resin. At most Hughes teaches a phosphonium salt permanently attached to a solid phase. This does not suggest Applicants' solid phase binding materials for capturing nucleic acids in a non-covalent and non-sequence specific manner having a cleavable linker portion linking the nucleic acid binding portion to the solid support.

2) The Examiner states:

> "One of ordinary skill in the art would have been motivated to make and use the chemistry of Hughes with the silica beads of Lough et al to take advantage of the chemical versatility afforded by orthogonal nucleic acid binding, as noted by Lough et al on page in column 5 lines 18-31".

In the first case there is no such concept of orthogonal nucleic acid binding in **Lough**, but rather "orthogonally cleavable linkers". Combining a quaternary phosphonium group with the teachings of **Lough** does not produce the presently claimed materials.

3) The rejection fails to state how the references are being used to modify one another. Specifically, the Examiner does not explain whether Hughes would somehow supply the phosphonium salt group missing from Lough for the purpose of binding or for linking. Clarification is requested. If it is assumed that the intent is to modify the immobilized nucleic acid binding beads of Lough by somehow incorporating the phosphonium salt traceless linkers of Hughes, such a modification fails to render the present materials obvious. The purpose of the materials of Lough is (column 2, lines 3-5)

> "the invention features novel compositions comprised of at least one bead conjugated to a solid support and further conjugated to at least one nucleic acid."

A preferred use of the composition of Lough is for the purpose of capturing target nucleic acids with selected sequence properties from a sample by sequence specific

hybridization. Any proposed modification of Lough for this use should therefore still result in a material with a conjugated nucleic acid for sequence-specific capture of nucleic acids. This teaches away from Applicants' solid phase binding materials for capturing nucleic acids in a non-covalent and non-sequence specific manner. The alternate embodiment of Lough has a covalent attachment group on the bead for covalently attaching an oligonucleotide. Any proposed modification of Lough for this use should therefore still result in a material with a covalent attachment group for covalently attaching an oligonucleotide or nucleic acid. Again, this teaches away from Applicants' solid phase binding materials for capturing nucleic acids in a non-covalent and non-sequence specific manner.

4) The rejection does not provide an explanation of how the commercial triphenylphosphine resin of Hughes would be adapted for use as a linker between either the solid support and bead of Lough or between the bead and capture nucleic acid of Lough. Nor does it explain how it could be done. Hughes provides no teaching for how such a resin could be linked to two materials.

For the reasons explained above Applicants maintain that no *prima facie* case of obviousness has been established and the rejection should be withdrawn.

Claims 1, 2, 4, 5, and 8 were rejected under 35 USC § 103(a) as being unpatentable over U.S. 5,900,481 to **Lough** and a paper (JACS, 104: 6551-5 (1982) **Tundo**). This rejection is traversed.

1) Tundo discloses silica-immobilized quaternary phosphonium groups as insoluble phase transfer catalysts. One of skill in the art would not be motivated to apply

the quaternary phosphonium groups of Tundo to the materials of Lough "for orthogonal nucleic acid binding". In the first case there is no such concept of orthogonal nucleic acid binding in Lough, but rather "orthogonally cleavable linkers". Combining a quaternary phosphonium group with the teachings of Lough does not produce the presently claimed materials.

2) The rejection fails to state how the references are being used to modify one another. Specifically, the Examiner does not explain whether Tundo would somehow supply the phosphonium salt group missing from Lough for the purpose of binding or for linking. Clarification is requested.

3) Neither reference, alone or in combination, teaches or suggests that quaternary phosphonium groups would be useful for nucleic acid binding. The argument that Lough teaches silica as "a support for binding nucleic acids" and that Tundo teaches silica-supported quaternary phosphonium salts begs the question.

4) The rejection does not provide an explanation of how the silica-trialkylphosphonium material of Tundo would be adapted for use as a linker between either the solid support and bead of Lough or between the bead and capture nucleic acid of Lough. Nor does it explain how it could be done. Tundo provides no teaching for how such a material could be linked to two materials.

For the reasons explained above Applicants maintain that no *prima facie* case of obviousness has been established and the rejection should be withdrawn.

Claims 1, 22 and 23 were rejected under 35 USC § 103(a) as being unpatentable over U.S. 5,900,481 to **Lough** and US Application 2003/0158333 to **Roberts**. This

rejection is traversed. Roberts describes water-soluble polymeric agents bearing a terminal thioester reactive group for covalent coupling to cysteine or histidine residues of proteins such as the protein component of a chromosome. These polymeric solubilizing agents contain an internal cleavable disulfide linkage for later removal of the polymer from the protein. Combining these two references fails to suggest or render obvious the materials of amended claims 1, 22, or 23 on several grounds.

1) The thioester group is not disclosed as the cleavable group in the materials of Roberts. Rather a disulfide group found elsewhere in the compounds functions as the cleavable group.

2) The materials of Roberts are designed to covalently attach to two specific amino acid residues of proteins. There is no basis in Roberts to provide any motivation to apply it to attracting nucleic acids non-covalently as specified in the present claims.

3) The reasoning of "orthogonal binding schemes" was raised. Again the Lough reference has been misapplied or misunderstood. There is no such concept of orthogonal nucleic acid binding in it, but rather of "orthogonally cleavable linkers". At most, the Roberts reference only discloses a thioester group, and even that not as the cleavable group. Roberts adds nothing in regard to nucleic acid binding. Neither it nor Lough discloses or suggests a cleavable nucleic acid binding group having a quaternary onium group (Claim 1), a thioester group linked to a benzylic quaternary onium group (Claim 22), or quaternary phosphonium group (Claim 23). Ignoring claim limitations renders the rejection improper.

All grounds for rejection having been addressed, and to the best of Applicants' knowledge overcome, Notice of Allowance is respectfully requested.

Richard Handley

Richard S. Handley, Ph.D.
Reg. No. 38,484